

What is claimed is:

1. An isolated nucleic acid molecule comprising a polynucleotide sequence having at least 85% identity with SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6

2. An isolated nucleic acid molecule according to claim 1, wherein the sequence identity is at least 90%.

3. An isolated nucleic acid molecule according to claim 1, wherein the sequence identity is at least 95%.

4. An isolated nucleic acid molecule according to claim 1, wherein said nucleic acid is a cDNA.

5. An isolated nucleic acid molecule according to claim 1, wherein said nucleic acid is a mammalian polynucleotide.

6. An isolated nucleic acid molecule according to claim 5, wherein said nucleic acid is a murine polynucleotide.

7. An isolated nucleic acid molecule according to claim 6, comprising SEQ ID NO:6.

8. An isolated nucleic acid molecule according to claim 7, wherein said nucleic acid is a human polynucleotide.

9. An isolated nucleic acid molecule according to claim 8, comprising SEQ ID NO:2 or SEQ ID NO:4.

10. An isolated nucleic acid molecule which encodes a polypeptide molecule comprising the amino acid sequence

PXCXXVXRCCGXXXCC (SEQ ID NO:1)

and having at least 85% identity with SEQ ID NO:3 or SEQ ID NO:5, or a fragment or analog thereof having the biological activity of PDGF-C.

11. An isolated nucleic acid molecule according to claim 10, wherein the amino acid sequence identity is at least 90%.

12. An isolated nucleic acid molecule according to claim 10, wherein the amino acid sequence identity is at least 95%.

13. An isolated nucleic acid molecule according to claim 10, which codes for a polypeptide which comprises a proteolytic site having the amino acid sequence RKSR or a structurally conserved amino acid sequence thereof.

14. A vector comprising a nucleic acid according to claim 1, which nucleic acid is operably linked with a promoter sequence.

15. A vector according to claim 14, wherein said vector is a eukaryotic vector.

16. A vector according to claim 14, wherein said vector is a prokaryotic vector.

17. A vector according to claim 14, wherein said vector is a plasmid.

18. A vector according to claim 14, wherein said vector is a baculovirus vector.

19. A method of making a vector which expresses a polypeptide comprising an amino acid sequence having at least 85% identity with SEQ ID NO:3 or SEQ ID NO:7, or fragment or analog thereof having the biological activity of PDGF-C, said method comprising incorporating an isolated nucleic acid according to claim 1 into said vector in operatively linked relation with a promoter.

20. A host cell transformed or transfected with a vector according to claim 14.

21. A host cell according to claim 20, wherein said host cell is a eukaryotic cell.

22. A host cell according to claim 20, wherein said host cell is a COS cell.

23. A host cell according to claim 20, wherein said host cell is a prokaryotic cell.

24. A host cell according to claim 20, wherein said host cell is a 293EBNA cell.

25. A host cell according to claim 20, wherein said host cell is an insect cell.

26. A host cell transformed or transfected with a vector comprising a nucleic acid sequence according to claim 1, operatively linked to a promoter, such that said host cell expresses a polypeptide comprising an amino acid sequence having at least 85% identity with SEQ ID NO:3 or SEQ ID NO:7, or a fragment or analog thereof having the biological activity of PDGF-C.

27. A means for amplifying a polynucleotide according to claim 1 in a test sample, said means comprising at least one pair of primers complementary to a nucleic acid according to claim 1.

28. A means for amplifying a polynucleotide according to claim 1 in a test sample, said means comprising a polymerase and at least one pair of primers complementary to a nucleic acid according to claim 1, for amplifying the polynucleotide by polymerase chain reaction in order to facilitate a sequence comparison of the polynucleotide with the nucleic acid according to claim 1.

29. An antibody specifically reactive with a polypeptide comprising an amino acid sequence having at least 85% identity with SEQ ID NO:3 or SEQ ID NO:7, or a fragment or analog thereof having the biological activity of PDGF-C, or a polypeptide produced by expression of a polynucleotide comprising a polynucleotide sequence having at least 85% identity with SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6, or of a polynucleotide which hybridizes under stringent conditions with SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6.

30. An antibody according to claim 29, wherein said antibody is a polyclonal antibody.

31. An antibody according to claim 29, wherein said antibody is a monoclonal antibody or a F(ab')<sub>2</sub>, F(ab'), F(ab) fragment or chimeric antibody.

32. An antibody according to claim 29, wherein said antibody is labeled with a detectable label.

33. An antibody according to claim 32, wherein said detectable label is radioactive isotope.

34. An antibody according to claim 31, wherein said monoclonal antibody is a humanized antibody.

35. A method of making a polypeptide comprising an amino acid sequence having at least 85% identity with SEQ ID NO:3 or SEQ ID NO:7, or a fragment or analog thereof having the biological activity of PDGF-C, or a polypeptide produced by expression of a polynucleotide comprising a polynucleotide sequence having at least 85% identity with SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6, or of a polynucleotide which hybridizes under stringent conditions with SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6, said method comprising the steps of:

culturing a host cell transformed or transfected with a vector comprising a polynucleotide encoding said polypeptide operably associated with a promoter sequence such that the nucleic acid sequence encoding said polypeptide is expressed; and

isolating said polypeptide from said host cell or from a growth medium in which said host cell is cultured.

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36. A method of stimulating growth of connective tissue or wound healing in a mammal, said method comprising administering to said mammal an effective growth stimulating amount of a polypeptide comprising an amino acid sequence having at least 85% identity with SEQ ID NO:3 or SEQ ID NO:7, or a fragment or analog thereof having the biological activity of PDGF-C, or a polypeptide produced by expression of a polynucleotide comprising a polynucleotide sequence having at least 85% identity with SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6, or of a polynucleotide which hybridizes under stringent conditions with SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6.

37. A method of making a vector which expresses a polypeptide comprising an amino acid sequence having at least 85% identity with at least amino acid residues 230 to 345 of SEQ ID NO:3 or of SEQ ID NO:7, said method comprising incorporating an isolated nucleic acid molecule encoding said amino acid residues into said vector in operatively linked relation with a promoter.

38. A method for producing an active truncated form of PDGF-C, comprising the step of expressing an expression vector comprising a polypeptide-encoding polynucleotide as claimed in claim 37.

39. A method for regulating receptor-binding specificity of PDGF-C, comprising the steps of expressing an expression vector comprising a polynucleotide encoding a polypeptide comprising an amino acid sequence having at least 85% identity with SEQ ID NO:3 or SEQ ID NO:7, or a fragment or analog thereof having the biological activity of PDGF-C, or a polypeptide produced by expression of a polynucleotide

comprising a polynucleotide sequence having at least 85% identity with SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6, or of a polynucleotide which hybridizes under stringent conditions with SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6, and supplying a proteolytic amount of at least one enzyme for processing the expressed polypeptide to generate the active truncated form of PDGF-C.

40. A method for selectively activating a polypeptide having a growth factor activity comprising the step expressing an expression vector comprising a polynucleotide encoding a polypeptide having a growth factor activity, a CUB domain and a proteolytic site between the polypeptide and the CUB domain, and supplying a proteolytic amount of at least one enzyme for processing the expressed polypeptide to generate the active polypeptide having a growth factor activity.

41. An isolated heterodimer comprising an active monomer of VEGF, VEGF-B, VEGF-C, VEGF-D, PDGF-C, PDGF-A, PDGF-B or PlGF and an active monomer of PDGF-C linked to a CUB domain.

42. An isolated heterodimer according to claim 41, further comprising a proteolytic site between the active monomer and the CUB domain linkage.

43. An isolated heterodimer comprising an active monomer of PDGF-C and an activated monomer of VEGF, VEGF-B, VEGF-C, VEGF-D, PDGF-C, PDGF-A, PDGF-B or PlGF linked to a CUB domain.

44. An isolated heterodimer according to claim 43, further comprising a proteolytic site between the activated monomer and the CUB domain linkage.

45. An isolated polynucleotide, comprising a polynucleotide sequence having at least 85% identity with SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6, or a polynucleotide which hybridizes under stringent conditions with SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6, and which encodes a sequence of amino acids comprising SEQ ID NO:1.

46. A method of promoting fibroblast mitogenesis in a mammal, comprising the step of administering to said mammal an effective fibroblast mitogenesis promoting amount of a polypeptide comprising an amino acid sequence having at least 85% identity with at least amino acid residues 230 to 345 of SEQ ID NO:3 or of SEQ ID NO:7.

47. A method of promoting fibroblast mitogenesis in a mammal, comprising administering to said mammal an effective fibroblast mitogenesis promoting amount of a polypeptide comprising an amino acid sequence having at least 85% identity with SEQ ID NO:3 or SEQ ID NO:7, or a fragment or analog thereof having the biological activity of PDGF-C, or a polypeptide produced by expression of a polynucleotide comprising a polynucleotide sequence having at least 85% identity with SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6, or of a polynucleotide which hybridizes under stringent conditions with SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6.



48. A method of inducing PDGF alpha receptor activation, comprising the step of adding a PDGF alpha-receptor stimulating amount of a polypeptide comprising an amino acid sequence having at least 85% identity with at least amino acid residues 230 to 345 of SEQ ID NO:3 or of SEQ ID NO:7.

49. A method of inducing PDGF alpha receptor activation, comprising the step of adding a PDGF alpha-receptor stimulating amount of a polypeptide comprising an amino acid sequence having at least 85% identity with SEQ ID NO:3 or SEQ ID NO:7, or a fragment or analog thereof having the biological activity of PDGF-C, or a polypeptide produced by expression of a polynucleotide comprising a polynucleotide sequence having at least 85% identity with SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6, or of a polynucleotide which hybridizes under stringent conditions with SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6.

50. A method of inhibiting tumor growth of a tumor expressing PDGF-C in a mammal, comprising administering to said mammal a PDGF-C inhibiting amount of a PDGF-C antagonist.

51. A method of identifying specific types of human tumors, comprising the step of taking a sample of the tumor and testing for the expression of PDGF-C.

52. The method of claim 51, wherein the specific types of tumors are selected from the group consisting of choriocarcinoma, Wilms tumor, megakaryoblastic leukemia, lung carcinoma and erythroleukemia.

53. A method for identifying an PDGF-C antagonist comprising:

admixing a substantially purified preparation of an activated truncated form of PDGF-C; and

monitoring, by any suitable means, an inhibition in the biological activity of PDGF-C.

54. A method for identifying an PDGF-C antagonist comprising:

admixing a substantially purified preparation of an full-length PDGF-C with a test agent; and

monitoring, by any suitable means, an inhibition in the cleavage of the CUB domain from PDGF-C.

55. A method for producing an activated truncated form of PDGF-C, comprising the steps of:

expressing an expression vector comprising a polynucleotide encoding a polypeptide comprising an amino acid sequence having at least 85% identity with SEQ ID NO:3 or SEQ ID NO:7, or a fragment or analog thereof having the biological activity of PDGF-C, or comprising a polynucleotide comprising a polynucleotide sequence having at least 85% identity with SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6, or a polynucleotide which hybridizes under stringent conditions with SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6, and

supplying a proteolytic amount of at least one enzyme for processing the expressed polypeptide to generate the activated truncated form of PDGF-C.

56. A method of inhibiting tissue remodeling during invasion of tumor cells into a normal population of cells, comprising administering to said mammal a PDGF-C inhibiting amount of a PDGF-C antagonist.

57. A method of treating fibrotic conditions in a mammal in need a such treatment, comprising administering to said mammal a PDGF-C inhibiting amount of a PDGF-C antagonist.

58. A method of claim 57, wherein the fibrotic conditions are found in the lung, kidney or liver.

59. A method of promoting angiogenesis in a bird or mammal, said method comprising administering to said bird or mammal an effective angiogenesis promoting amount of a polypeptide comprising a sequence of amino acids having at least 85% identity with at least amino acid residues 230 to 345 of SEQ ID NO:3 or of SEQ ID NO:7.

60. A method according to claim 59, wherein said polypeptide is administered in the form of a dimer.